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U.S. Army Environmental Hygiene Agency

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PHASE 3
PRELIMINARY ASSESSMENT OF THE ORAL TOXICITY
OF 1,5-DIAZIDO-3-NITRAZAPENTANE
2- AND 6-WEEK FEEDING STUDY, MALE AND FEMALE RATS
STUDY NO. 75-51-Y809-90
MAY 1991 - SEPTEMBER 1992

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-5422

REPLY TO
ATTENTION OF

HSHB-MO-T (40)

4 May 1993

MEMORANDUM FOR Commander, U.S. Army Materiel Command, ATTN: AMCSG-I (Mr. Svalina), 5001 Eisenhower Avenue, Alexandria, VA 22333-0001

SUBJECT: Phase 3 - Preliminary Assessment of the Oral Toxicity of 1,5-Diazido-3-Nitrazapentane, 2-and 6-Week Feeding Study, Male and Female Rats, Study No. 75-51-Y809-90, May 1991 - September 1992

Ten copies of the subject report with Executive Summary are enclosed.

FOR THE COMMANDER:

MAURICE H. WEEKS
Chief, Toxicology Division

Encl

CF (w/encl):
CDR, AMCCOM, ATTN: AMSMC-SG
CDR, HSC, ATTN: HSCL-P
CDR, AMEDDC&S, ATTN: HSHA-MP
CDR, USAMMDA, ATTN: SGMMA-MP
DIR, ADV CEN DIV TOX, NRC (2 cy)
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17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	1,5-Diazido-3-Nitrazapentane (DANPE) Gavage Testicular Hypospermatogenesis, insterstitual inflammation No-observed-adverse-effect-level (NOAEL), Feeding study

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

A 2 and 6 week gavage feeding of DANPE caused testicular hypospermatogenesis in male rats and pneumonitis in female rats. A NOAEL was not achieved in male rats but was achieved in female rats at the 56.00 mg/kg/day dose level.

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-5422

REPLY TO ATTENTION OF

EXECUTIVE SUMMARY
PHASE 3
PRELIMINARY ASSESSMENT OF THE ORAL TOXICITY OF 1,5-DIAZIDO-3-NITRAZAPENTANE
2- AND 6-WEEK FEEDING STUDY, MALE AND FEMALE RATS
STUDY NO. 75-51-Y809-90
MAY 1991 - SEPTEMBER 1992

1. GENERAL. A Preliminary Assessment of the Oral Toxicity of 1,5-Diazido-3-Nitrazapentane (DANPE) for a 2- and 6-Week Feeding Study with another rodent species; male and female rats was completed September 1992. The report is enclosed.

2. ESSENTIAL FINDINGS. A 2- and 6-week gavage feeding of DANPE solutions has the potential to cause testicular hypospermatogenesis in male rats and pneumonitis in female rats. A no-observed-adverse-effect level was achieved in female rats at the 56.00 mg/kg/day dose level but not in male rats.

3. RECOMMENDATIONS. The following paragraphs are recommendations based on professional scientific judgment:

a. Although DANPE is not a primary skin irritation, caution should be taken to prevent DANPE solutions from skin contact because of its potential to cause the previously mentioned problems in paragraph 2, above. Flush immediately with large volumes of water should skin contamination occur. Do not use abrasive soap, this may increase absorption through the skin.

b. Protective clothing should be worn by workers when contact is possible and splash guards in place to prevent splashing onto individuals or equipment being handled.

c. Based on the findings of testicular hypospermatogenesis in this mammalian species, extreme caution should be taken when handling this compound and avoid all exposure.

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PRELIMINARY ASSESSMENT OF THE ORAL TOXICITY OF 1,5-DIAZIDO-3-NITRAZAPENTANE
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STUDY NO. 75-51-Y809-90
MAY 1991 - SEPTEMBER 1992

1. REFERENCES. See Appendix A for a list of references.

2. AUTHORITY. Memorandum, 1st End, AMC, 31 Oct 88, AMCSG-I, Subject: Toxicity Study.

3. PURPOSE. This subchronic study was designed to examine the oral toxic effects associated with a short term exposure of 1,5-Diazido-3-Nitrazapentane (DANPE) to male and female rats. The results will provide more information on possible target organs/systems; a no-observed-adverse-effect-level (NOAEL); establish a dose-response order of toxicity for DANPE and aid the occupational health physician in establishing preliminary guidelines for safe workplace conditions.

4. BACKGROUND.

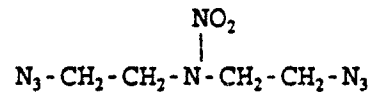
a. The DANPE, a flammable liquid, is of interest to the U.S. Army for use as an energetic material. No referenced toxicology information on this material was found in searches performed on the National Library of Medicine's Toxicology data network as listed in the Hazardous Substances Databank and in the Registry of Toxic Effects of Chemical Substances.

b. Previous evaluation of this compound in the Toxicology Division suggests an oral approximate lethal dose (ALD) value in male rats 1498 mg/kg and female rats 617 mg/kg. The DANPE has a dermal ALD toxicity of 3192 mg/kg for female rabbits and 2129 mg/kg in male rabbits. The DANPE has a primary eye irritant classification of "c," producing mild injury to the cornea. In addition, some injury to the conjunctiva was found. It has a skin irritant classification of "I," producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. The DANPE produced no sensitization reaction in guinea pigs (reference 1). A 90-day dermal application of DANPE has the potential to cause testicular hypospermatogenesis in male rabbits and the inhibition of mature ovarian follicle formation in female rabbits. A NOAEL of 27.3 mg/kg/day dose level was achieved in female rabbits but not in male rabbits (reference 2).

5. MATERIALS.

a. The DANPE solutions have a slightly irritating odor because of their solvent, ethyl acetate. The sample Lot #2316-C with a stated concentration of 37 percent DANPE was obtained from Naval Ordnance Station, Indian Head, Maryland. The batch sample was analyzed using the Digilab® FTS-15/90 Fourier Transform Infrared Spectrometer filtered with an Mercury-Cadmium-Telluride detector (Appendix B). The chemical structure of DANPE is as follows:

DANPE



b. Ethyl acetate is nontoxic and has a characteristic fruity odor and pleasant taste when diluted; therefore, it is primarily used as fruit essences. Pertinent information regarding the mutagenicity, teratogenicity and carcinogenicity was located in the Integrated Risk Information System.

c. This report and data generated in these studies are stored in Toxicology Division files, which are located in the basement of Building E1570, Aberdeen Proving Grounds, Edgewood Area, MD 21010-5422.

d. 2- and 6-Week Range-Finding Repeat Oral Study: Male and Female Rats.

*(1) This 2- and 6-week oral feeding study was performed in rats according to the Toxicology Division's Standing Operating Procedure for 14-Day Range Finding and 90-Day Feeding Study in Rats (reference 3).

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*Studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Care. In conducting the studies in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," U.S. Department of Health, Education and Welfare Publication No. (NIH) 86-23 revised 1985.

(2) For this study, 150 rats, 72 male and 78 female were used. They were randomly selected into 7 groups of either 12 or 6 male and female per group. These five dosage groups; 250 mg/kg/day, 125 mg/kg/day, 62.5 mg/kg/day, 31.3 mg/kg/day, and 15.6 mg/kg/day were a fraction of the determined concentration (Approximately 500 mg/kg) of the DANPE solution plus a solvent and a cage control groups (Table 1). The rats were between 5 to 6 weeks of age and 150-350 grams in weight. This study was designed to determinate the toxic effects associated with repeated oral ingestion of DANPE and its solvent, ethyl acetate, over a limited period of time. The test provides information on target organs, possibilities of accumulation and effect and the NOAELs.

TABLE 1. PREDICTED DAILY DOSES (2- and 6-WEEK FEEDING STUDY) DANPE

Group No.	Male Rats	Female Rats	Fraction of (500 MG/KG) Concentration
1	250 Mg/Kg/Day	250 Mg/Kg/Day	1/2x
2	125 Mg/Kg/Day	125 Mg/Kg/Day	1/4x
3	62.5 Mg/Kg/Day	62.5 Mg/Kg/Day	1/8x
4	31.3 Mg/Kg/Day	31.3 Mg/Kg/Day	1/16x
5	15.6 Mg/Kg/Day	15.6 Mg/Kg/Day	1/32x
6	Ethyl acetate	Ethyl acetate	250 Mg/Kg/Day
7	Control	Control	(0) Mg/Kg/Day

(3) Dosage levels for the seven test groups of each sex were fractions of the concentration value determined for DANPE from the oral ALD. Table 1 shows daily doses for the test. The calculated dose was given to the test animals by gavage daily for 5 days per week for a 2 or 6 week dosing period. Individual animals' weight was determined prior to the initial dosing, weekly, and at death. Weekly weights were used to calculate the delivered dosage to be gavaged for that week.

(4) Animals to be bled for clinical and hematology analysis were randomly selected prior to dosing. Blood samples were taken and analyzed before and after exposure for comparison purposes.

(5) Appropriate action was taken to minimize the loss of animals during the study (e.g., refrigeration and necropsy of animals found dead, and sacrifice of weak or moribund animals with subsequent necropsy).

(6) On the final day of the study, blood samples were collected by intracardiac puncture under CO_2 anesthesia with follow-on CO_2 euthanasia. Tables 2 and 3 list the clinical chemistry and hematological parameters. After which, the rats were sacrificed and necropsied with appropriate histopathological examinations carried out.

6. RESULTS.

a. 2-Week Gavage.

(1) Tables 4 and 5 show the predicted verses actual daily doses each group received.

TABLE 2. CLINICAL CHEMISTRY

Serum Glutamic Oxaloacetic Transaminase (Aspartate Aminotransferase)	(SGOT)	(AST)
Serum Glutamic Pyruvic Transaminase (Alanine Aminotransferase)	(SGPT)	(ALT)
Alkaline Phosphatase	(ALK.PHOS.)	
Glucose		
Blood Urea Nitrogen	(BUN)	
Total Protein		
Cholesterol		
Creatine Phosphokinase	(CPK)	
Triglycerides		
Total Bilirubin		
Lactic Dehydrogenase	(LDH)	
Prothrobin Times		

TABLE 3. HEMATOLOGY

Hematocrit
Hemoglobin
Erythrocyte Count
Total and Differential Leukocyte Counts
Mean Cell Volume
Mean Cell Hemoglobin
Mean Cell Hemoglobin Concentration

TABLE 4. PREDICTED VERSES ACTUAL DAILY DOSE (MG/ML/DAY) (2-WEEK FEEDING STUDY) DANPE SOLUTIONS (MALE RATS)

PREDICTED	250	125	62.5	31.3	15.6	*SOL. CONT.	CONT
ACTUAL	317	132	74.3	39.7	21.3	250	0

*Ethyl acetate (250 mg/ml/day).

TABLE 5. PREDICTED VERSES ACTUAL DAILY DOSE (MG/ML/DAY) (2-WEEK FEEDING STUDY) DANPE SOLUTIONS (FEMALE RATS)

PREDICTED	250	125	62.5	31.3	15.6	*SOL. CONT.	CONT
ACTUAL	206	98.8	47.5	28.5	15.3	250	0

*Ethyl acetate (250 mg/ml/day).

(2) Test data collected during this 2-week feeding study (body weights, organ-to-body weight ratios, organ-to-brain weight ratios, and blood chemistry values) were statistically compared with the data from their respective control groups using the student "t" test at the 0.05 level of significance (Appendices C-L).

(3) The blood hematology values revealed a decrease in the white blood cells for the female rats in the 250 and 125 mg/kg/day dosage groups when compared to the control group (Appendix C). Male rats showed no significant changes from the control group (Appendix D).

(4) The clinical chemistry values (Appendices E and F) showed significant changes in all dosage groups for both male and female rats when compared to their respective control groups.

(5) Significant decreases occurred in mean terminal body weights for only the male rats when compared to the control group. The female rats showed no significance in terminal body weights when compared with the control group (Appendices G and J).

(6) Significant organ-to-body weight ratio differences were demonstrated in the kidneys, heart, brain, adrenals and the testes of male rats 250, 62.5 and the ethyl acetate 250 mg/kg/day dosage groups. The female rats showed significant differences in the livers and kidneys of the 250 and 125 mg/kg/day dosage groups and the brain of the 250 mg/kg/day group when compared to their respective control groups (Appendices H and L). The organ-to-brain weight ratio differences were demonstrated in the spleen and heart of the high 250 mg/kg/day and the liver and heart of the ethyl acetate 250 mg/kg/day dosage group male rats. The only significance for female rats was demonstrated in the liver weights of the 250 and 125 mg/kg/day dosage groups when compared to their respective control groups (Appendices I and K).

b. <u>6-Week Gavage</u>.

(1) Tables 6 and 7 show the predicted verses actual daily doses each group received.

(2) Test data collected during this 6-week feeding study (body weights, organ-to-body weight ratios, organ-to-brain weight ratios, and blood chemistry values) were statistically compared with the data from their respective control groups using the student "t" test at the 0.05 level of significance (Appendices M-V).

(3) Dose-related significant increases were noted in body-to-organ weight ratios (Appendices O and R). The male rats showed significant decrease in the testes weights (Figure 1) and an increase in the brain weights for the 250, 125 and the 62.5 mg/kg/day dosage groups when compared to their respective control group (Appendix O). The female rats showed a significant increase in liver weights for the 250 and 125 mg/kg/day dosage

Phase 3, Toxicological Study No. 75-51-Y809-90, May 91 - Sep 92

TABLE 6. PREDICTED VERSES ACTUAL DAILY DOSE (MG/ML/DAY) (6-WEEK FEEDING STUDY) DANPE SOLUTIONS (MALE RATS)

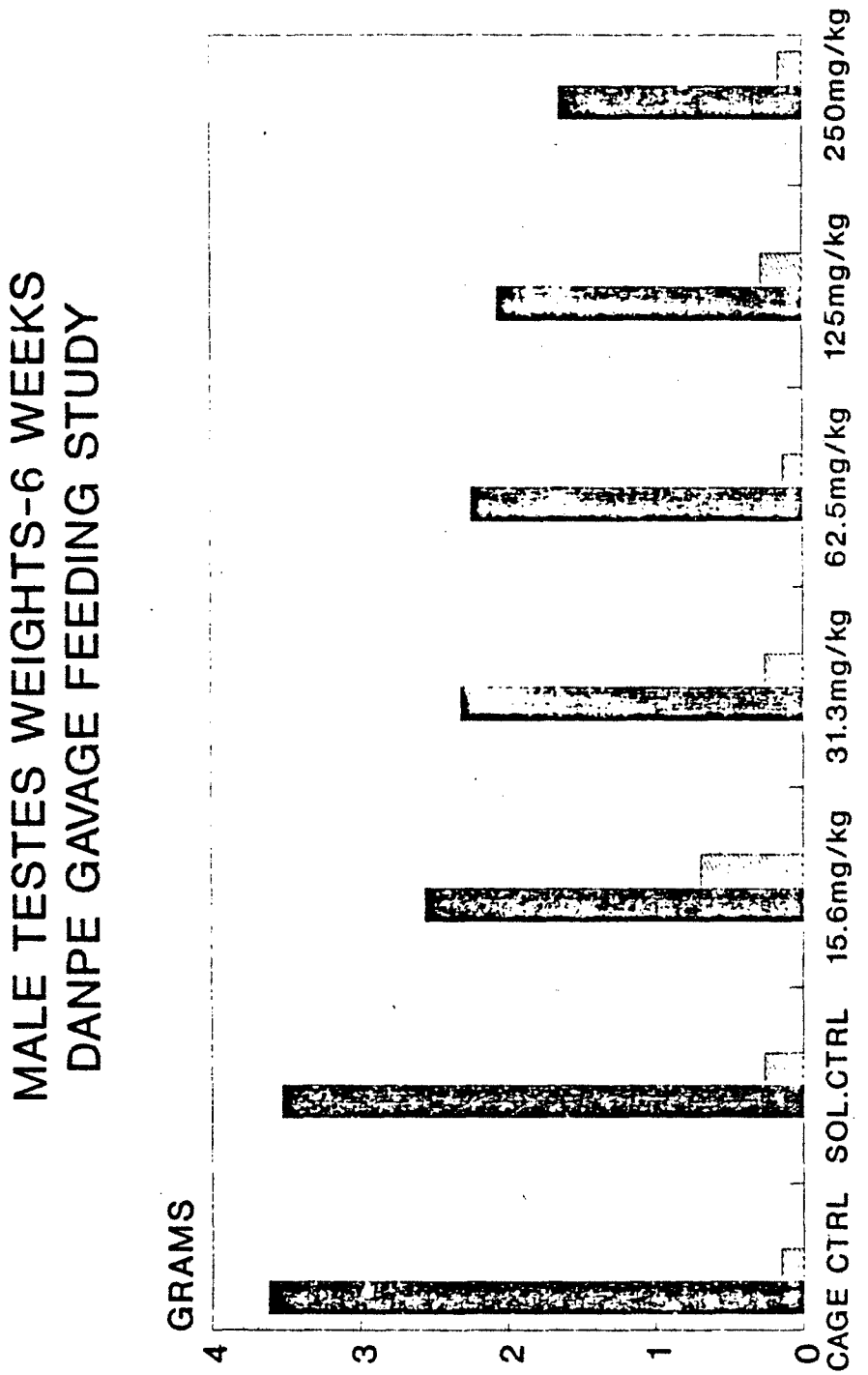
PREDICTED	250	125	62.5	31.3	15.6	*SOL. CONT.	CONT
ACTUAL	277.5	128.5	69.9	37.1	20.8	250	0

* Ethyl acetate (250 mg/ml/day).

TABLE 7. PREDICTED VERSES ACTUAL DAILY DOSE (MG/ML/DAY) (6-WEEK FEEDING STUDY) DANPE SOLUTIONS (FEMALE RATS)

PREDICTED	250	125	62.5	31.3	15.6	*SOL. CONT.	CONT
ACTUAL	212.7	108.00	56.00	31.4	16.9	250	0

*Ethyl acetate (250 mg/ml/day).



75-51-0809-90

Figure 1.

groups when compared to their respective control group (Appendix R). Brain weight increases were also noted in the 250, 62.5 and the 15.6 mg/kg/day dosage groups (Appendix R). No significance was demonstrated in the female ovaries (Figure 2).

(4) Daily oral gavaging of DANPE in male rats was associated with a high incidence of testicular hypospermatogenesis in animals that received 62.5, 125 and 250 mg/kg/day of the test material. There were no microscopically discernible testicular alterations in the terminal kill rats that received 250 mg/kg/day ethyl acetate or a lower dosage of DANPE solution, or in any of the interim kill rats. Testicular hypospermatogenesis was not observed in the untreated control males. There was associated with DANPE an increased incidence of interstitial inflammation in the lungs of female rats from the 62.5, 125, and 250 mg/kg/day terminal kill groups. Rats receiving 250 mg/kg/day ethyl acetate had similarly elevated incidence of interstitial inflammation of the lung (reference 4).

(5) Blood clinical chemistry values (Appendices S and T) demonstrated significant changes when compared to their respective control groups.

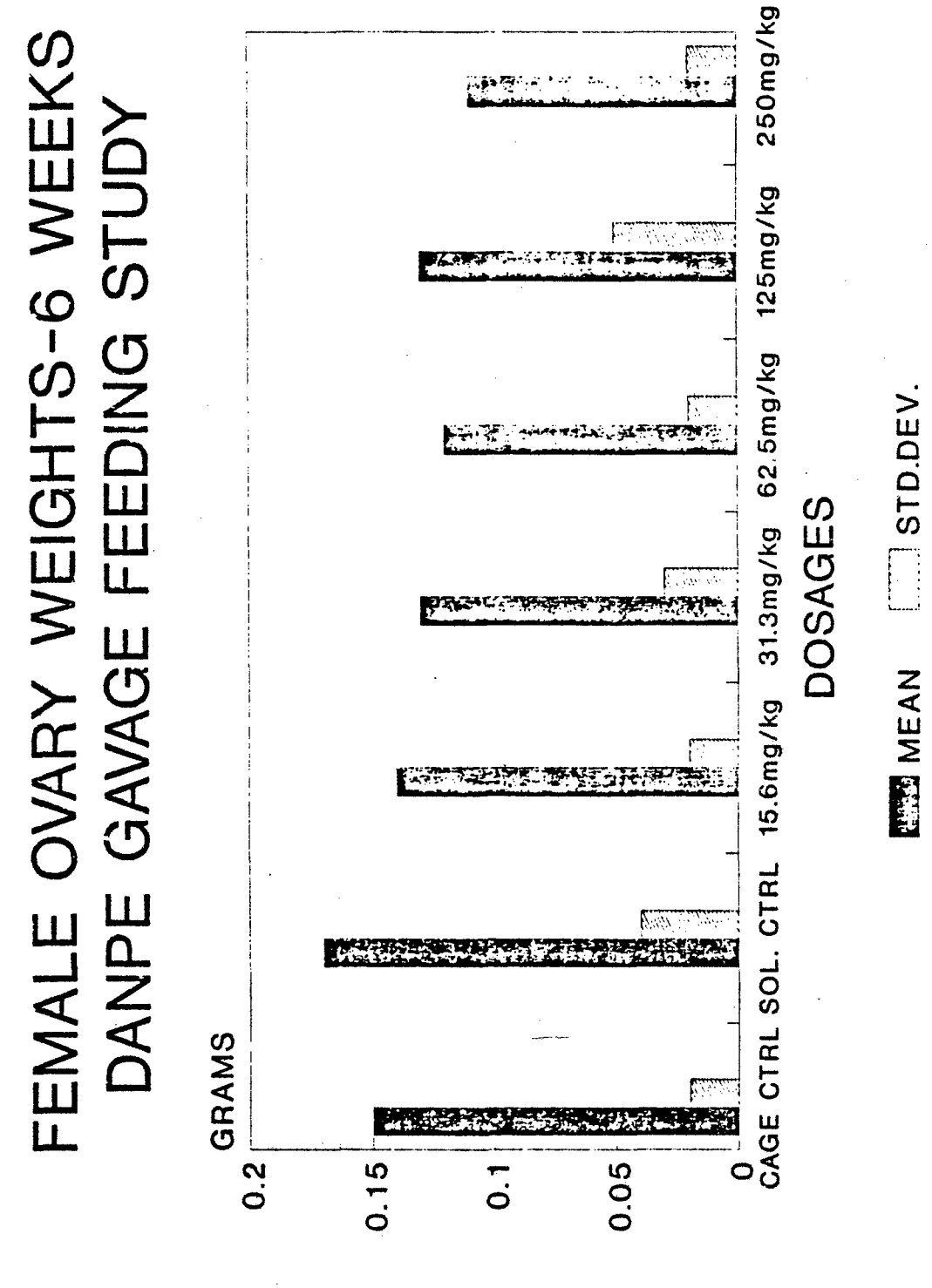
(6) The blood hematology values revealed a decrease in red blood cells, hemoglobin, and hematocrit for both female and male rats in the high dose group (Appendices U and V).

7. DISCUSSION.

a. The results of the 2- and 6-week subchronic oral ingestion of Danpe solutions show this compound causes testicular hypospermatogenesis in the male rats and only an increased incidence of interstitial inflammation of the lungs in female rats (reference 4).

b. Sporadic differences in the various clinical chemistry and hematology values suggests no dose related response. The hematology analysis showed in the high dose group for male and female rats a decrease in red blood cells and hemoglobin values. This could possibly be associated with the incidence of sequestered blood in the lymph nodes, suggesting hemorrhage (reference 4). An increase in the white blood cells were also noted, a possible response to the compound and its solvent since white blood cells act to defend the body against foreign substances (reference 5).

c. The results from these studies suggest an oral NOAEL of 56.00 mg/kg/day dose level was achieved in the female rats but not for male rats.



75-51-0809-90

Figure 2.

8. RECOMMENDATIONS.

a. Use extreme caution to prevent DANPE solutions from skin contact. Flush immediately with large volumes of water should skin contamination occur. Do not use abrasive soap, this may increase absorption through the skin.

b. Wear protective clothing when contact is possible, and keep splash guards in place to prevent splashing onto individuals or equipment being used.

c. Prevent all potential exposure of this compound to male workers since testicular hypospermatogenesis was demonstrated in two mammalian species by two different routes of exposure.

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APPROVED:

MAURICE H. WEEKS
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APPENDIX A

REFERENCES

1. Phase 1, Preliminary Assessment of the Relative Toxicity of 1,5-Diazido-3-Nitrazapentane (DANPE) Acute Toxicity, Study No. 75-51-0856-91, February 1992.

2. Phase 2, Preliminary Assessment of the Relative Toxicity of 1,5-Diazido-3-Nitrazapentane, 90-Day Dermal Application Male and Female Rabbits, Study No. 75-51-Y809-90, June 1992.

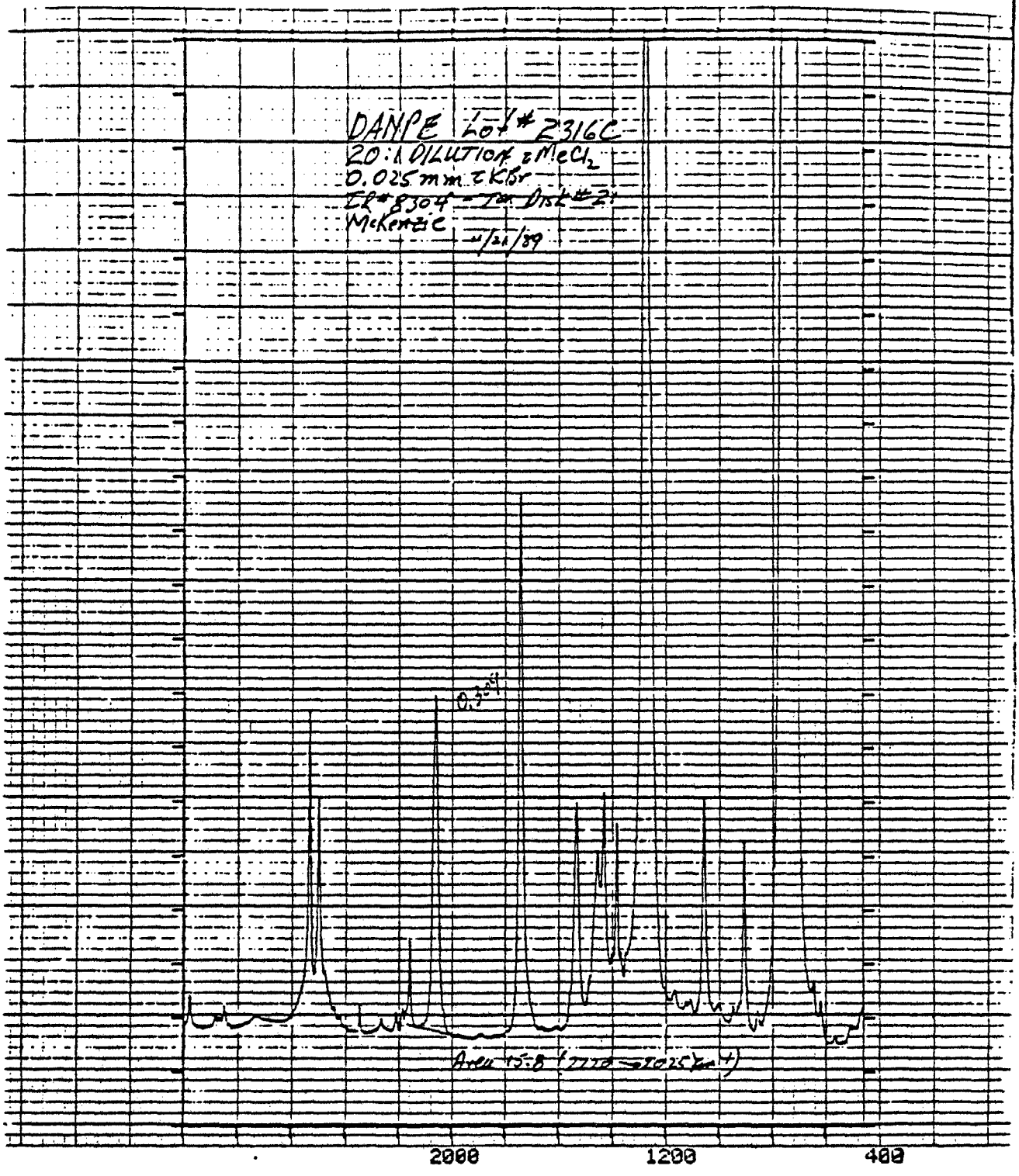
3. SOP No. 37.92, HSHB-MO-T, subject: 14-Day Range Finding and 90-Day Feeding Study in Rats.

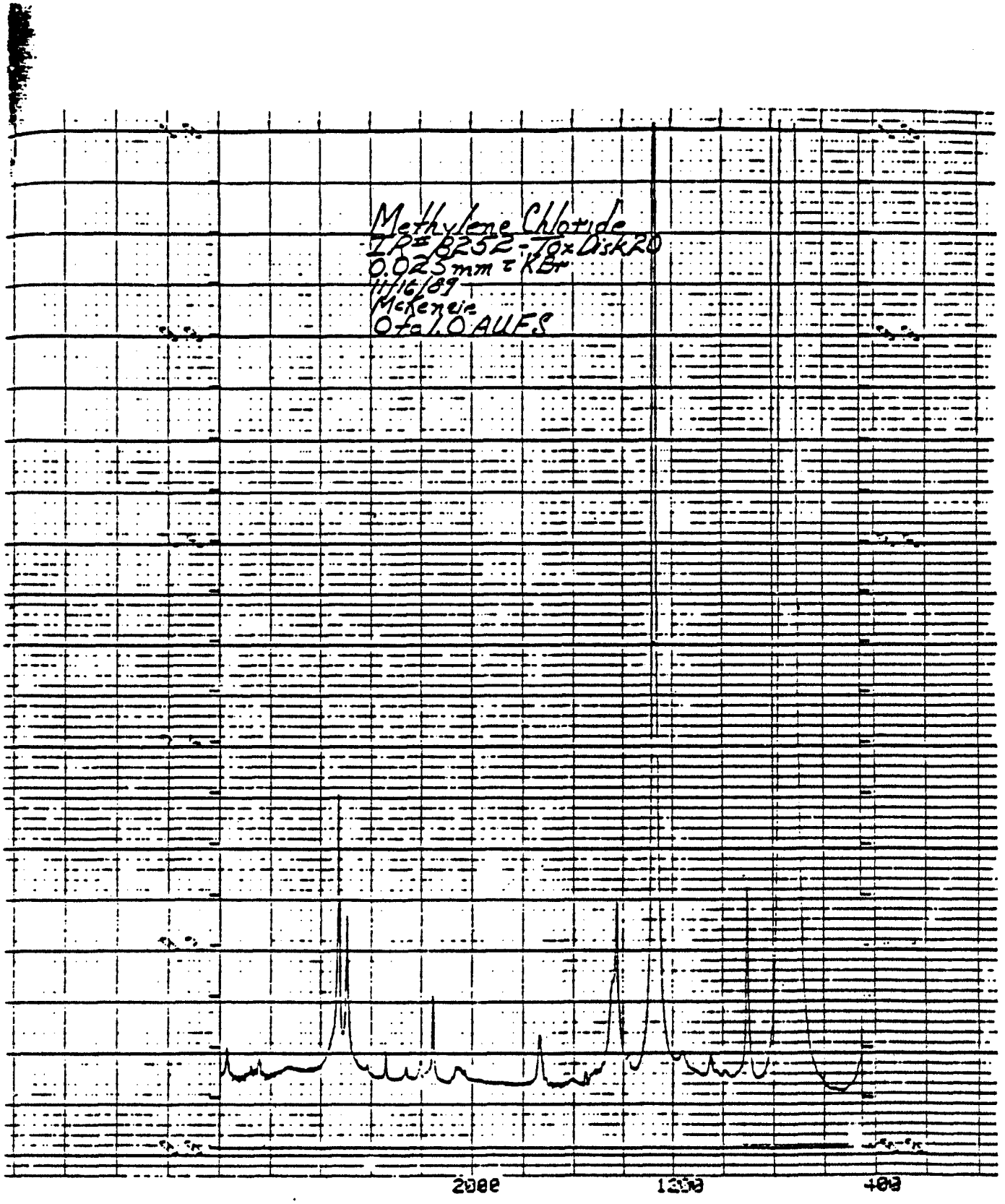
4. Report: 12 November 1991, George A. Parker, D.V.M., LTD. 111-A Carpenter Drive, P.O. Box 1278, Sterling, Virginia 22170-8424, subject: Final Pathology Report, 1,5-Diazido-3-Nitrazapentane (DANPE) 42-Day Range-Finding Repeat Oral Study in Male and Female Rats; Study No. 75-51-0856-91.

5. Henry, J.B., Clinical Diagnosis and Management by Laboratory Methods, 16th ED., W.B. Saunders Company, 1979.

APPENDIX B

SPECTRA DIAGRAM OF DANPE LOT NO. 2316C


DAMPE Lot # 2316C
20:1 DILUTION in $MeCl_2$
0.025 mm in KBr
ER#8304 - Tan Disk #2
McKenzie 11/21/89
0.3%
Area 15.8 (min = 2025 cm⁻¹)
2000
1200
400



Reference Material Spectra

APPENDIX C

2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
HEMATOLOGY - FEMALE RATS

DOSAGE Predicted (Actual)	RBC 10/µl	HCT %	MCV fl	WBC 10/µl	HGB g/dl	MCH pg	MCHC g/dl
250 MG/KG (206)	6.67 +0.27	40.02 +-1.23	57.57 +-1.75	6.78 *+-1.46	14.20 +-0.53	20.43 +-0.65	35.50 +-0.56
125 MG/KG (98.8)	6.63 +-0.39	39.23 +-2.58	59.13 +-1.09	4.90 *+-1.81	14.02 +-0.85	21.13 +-0.44	35.75 +-0.56
62.5MG/KG (47.5)	7.08 +-0.22	41.80 +-0.84	58.72 +-1.68	9.94 +-0.74	14.94 +-0.43	20.98 +-0.38	35.74 +-0.63
15.6 MG/KG (15.3)	7.55 +-0.14	43.57 *+-1.34	57.72 +-1.72	9.57 +-4.10	15.68 *+-0.38	20.77 +-0.48	36.00 +-0.30
ETHACET.CON (250)	7.30 +-0.31	42.73 +-2.33	58.53 +-1.43	12.62 +-2.76	15.35 +-0.76	21.03 +-0.52	35.93 +-0.40
CONTROL (0)	7.02 +-0.23	40.72 +-1.08	58.08 +-2.57	8.30 +-2.40	14.66 +-0.39	20.92 +-1.00	35.98 +-0.31

* = Stratistical Significance at the p >0.05 Level.
RBC = RED BLOOD CELLS
HGB = HEMOGLOBIN
HCT = HEMATOCRIT
MCV = MEAN CELL VOLUME
MCH = MEAN CELL HEMOGLOBIN
MCHC = MEAN CELL HEMOGLOBIN CONCENTRATION
WBC = WHITE BLOOD CELL

APPENDIX D

2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
HEMATOLOGY - MALE RATS

DOSAGE Predicted (Actual)	RBC 10/µl	HCT %	MCV fl	WBC 10/µl	HGB g/dl	MCH pg	MCHC g/dl
250 MG/KG (317)	7.18 +0.32	40.95 +-1.29	57.05 +-1.51	9.93 +-1.96	14.52 +-0.49	20.23 +-0.47	35.45 +-0.46
6.25 MG/KG (74.3)	7.18 +-0.46	42.17 +-2.64	58.73 +-1.77	13.55 *+-4.31	14.90 +-0.90	20.73 +-0.70	35.33 +-0.37
15.6 MG/KG (21.3)	7.18 +-0.66	42.28 +-2.98	58.95 +-1.67	8.28 +-1.91	14.83 +-0.96	20.70 +-0.64	35.12 +-0.44
ETHACET.CON (250)	7.00 +-0.62	42.28 +-1.84	60.37 +-4.41	9.27 +-3.05	14.80 +-0.84	21.08 +-0.91	35.02 +-1.62
CONTROL (0)	6.87 +-0.37	40.50 +-2.50	59.72 +-1.46	11.82 +-4.00	14.18 +-0.79	20.92 +-0.37	35.03 +-0.71

* = Statistical Significance at the p >0.05 Level.
RBC = RED BLOOD CELLS
HGB = HEMOGLOBIN
HCT = HEMATOCRIT
MCV = MEAN CELL VOLUME
MCH = MEAN CELL HEMOGLOBIN
MCHC = MEAN CELL HEMOGLOBIN CONCENTRATION
WBC = WHITE BLOOD CELL

APPENDIX E

2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
CLINICAL CHEMISTRY - MALE RATS

DOSAGE Predicted (Actual)	ALK.PHOS IU/L	SGOT IU/L	SGPT IU/L	GLUCOSE IU/L	T.BILI MG/DL	BUN MG/DL	TOT.PROT. G/DL	CHOLESTEROL IU/L	TRIGLYCERIDES IU/L
250 MG/KG (317)	452.20 +-193.5	78.30 *+-10.8	31.50 *+-3.1	146.70 *+-8.2	0.37 *+-0.08	20.60 +-3.3	6.60 +-0.39	61.61 *+-7.97	206.20 *+-43.5
62.5 MG/KG (74.3)	449.30 +-118.3	95.40 +-16.1	40.30 +-7.8	153.90 +-41.3	0.41 *+-0.06	18.10 +-2.1	6.88 +-0.48	66.02 *+-7.21	222.10 *+-36.8
15.6 MG/KG (21.3)	396.20 +-60.2	85.80 +-10.2	47.20 +-12.0	140.20 +-15.3	0.52 +-0.11	18.65 +-1.32	7.10 +-0.15	77.22 +-9.74	255.10 *+-49.1
ETHYLACET (250 MG/KG)	548.60 +-191.4	106.80 +-11.8	46.80 +-7.2	118.10 +-13.3	0.50 *+-0.10	17.42 *+-1.2	6.60 +-0.17	75.24 +-8.26	307.10 +-96.3
CONTROL (0)	437.80 +-107.6	98.10 +-16.3	41.70 +-5.8	124.90 +-7.5	0.65 +-0.13	20.20 +-1.33	7.03 +-0.50	84.36 +-18.43	330.90 +-59.8

* = Statistical Significance at the p >0.05 Level.
ALK.PHOS.=ALKALINE PHOSPHATASE
SGOT=SERUM GLUTAMIC OXALOACETIC TRANSAMINASE
SGPT=SERUM GLUTAMIC PYRUVIC TRANSAMINASE
GLUCOSE
T.BILL.=TOTAL BILIRUBIN
BUN=BLOOD UREA NITROGEN
TOT.PROT.=TOTAL PROTEIN
CHOLESTEROL
TRIGLYCERIDES

APPENDIX F

2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
CLINICAL CHEMISTRY - FEMALE RATS

DOSAGE Predicted (Actual)	ALK.PHOS IU/L	SGOT IU/L	SGPT IU/L	GLUCOSE IU/L	T.BILI MG/DL	BUN MG/DL	TOT.PROT. G/DL	CHOLESTEROL IU/L	TRIGLYCERIDES IU/L
250 MG/KG (206)	394.20 *+-127.30	74.80 *+-9.30	39.20 *+-5.90	145.90 *+-8.90	0.47 +-0.06	20.50 +-2.00	7.60 +-0.50	75.20 *+-9.60	205.40 *+-43.50
125 MG/KG (98.8)	359.00 *+-23.80	83.50 *+-7.60	31.20 +-4.70	145.60 *+-8.50	0.43 +-0.05	22.50 +-8.90	7.30 +-0.60	73.40 *+-12.00	180.30 *+-19.60
62.5 MG/KG (47.5)	412.70 *+-67.90	102.40 *+-35.30	39.50 *+-5.40	145.70 +-25.6	0.52 *+-0.07	22.70 +-5.90	7.40 +-0.40	78.70 +-12.20	239.70 *+-35.50
156. MG/KG (15.3)	336.30 *+-45.70	112.90 *+-32.70	33.40 *+-4.90	149.50 +-34.10	.048 +-0.08	23.10 +-2.60	7.40 +-0.30	78.20 +-12.20	208.70 +-27.20
ETHYLACET (250 MG/KG)	419.60 *+-110.40	125.90 *+-115.20	34.60 *+-7.50	181.70 +-26.80	0.48 +-0.10	19.60 +-2.80	7.30 +-0 30	90.70 +-13.90	236.80 *+-36.90
CONTROL (0)	255.30 +-60.90	59.40 +-7.90	26.39 +-3.00	136.10 +-4.40	0.43 +-0.06	23.20 +-3.60	7.70 +-0.40	85.70 +-7.50	188.80 +-32.70

* = Statistical Significance at the p >0.05 Level
ALK.PHOS.=ALKALINE PHOSPHATASE
SGOT=SERUM GLUTAMIC OXALOACETIC TRANSAMINASE
SGPT=SERUM GLUTAMIC PYRUVIC TRANSAMINASE
GLUCOSE
T.BILL.=TOTAL BILIRUBIN
BUN=BLOOD UREA NITROGEN
TOT.PROT.=TOTAL PROTEIN
CHOLESTEROL
TRIGLYCERIDES

APPENDIX G

RATS 2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
MALE
TERMINAL WEIGHTS (GMS)

DOSAGE PREDICTED ACTUAL	250 MG/KG (317)	62.5 MG (74.3)	15.6 MG/KG (21.3)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER	18.49 +-1.57	18.04 +-2.62	17.37 +-2.22	14.91 *+-1.34	20.51 +-2.40
KIDNEY	3.43 +-0.25	3.33 +-0.27	3.02 +-0.28	3.02 +-0.28	3.49 +-0.22
SPLEEN	0.75 *+-0.12	1.06 +-0.28	0.84 +-0.24	0.93 +-0.05	0.87 +-0.06
HEART	1.34 *+-0.12	1.48 +-0.14	1.34 *+-0.09	1.31 *+-0.08	1.52 +-0.07
TESTES	3.06 +-0.15	3.06 +-0.26	3.09 +-0.21	3.12 +-0.23	3.27 +-0.21
ADRENAL	0.06 +-0.01	0.06 +-0.01	0.05 +-0.01	0.06 +-0.01	0.05 +-0.01
BRAIN	2.04 +-0.05	2.05 +-0.09	2.01 +-0.10	1.98 +-0.08	2.06 +-0.04
BODY WTS	336.8 *+-13.67	356.3 *+-26.5	360.3 *+-29.7	309.7 *+-53.69	401.3 +-21.77

* Significantly different from control at the 0.05 level of probability.

APPENDIX H

RATS 2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
MALE ORGAN TO BODY WEIGHT RATIOS (GMS)
% OF BODY WEIGHT

DOSAGE PREDICTED ACTUAL	250 MG/KG (317)	62.5 MG (74.3)	15.6 MG/KG (21.3)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER	5.49 +-0.32	5.04 +-0.40	4.81 +-0.30	4.59 *+-0.51	5.10 +-0.43
KIDNEY	1.02 *+-0.07	0.94 +-0.06	0.86 +-0.09	0.93 +-0.05	0.87 +-0.06
SPLEEN	0.22 *+-0.03	0.3 +-0.06	0.23 +-0.05	0.26 +-0.06	0.27 +-0.04
HEART	0.4 +-0.05	0.42 *+-0.02	0.37 *+-0.03	0.40 *+-0.02	0.38 +-0.02
TESTES	0.91 *+-0.05	0.86 +-0.06	0.86 +-0.06	0.96 *+-0.08	0.82 +-0.07
BRAIN	0.61 *+-0.03	0.58 *+-0.04	0.56 +-0.05	0.61 *+-0.05	0.52 +-0.03
ADRENALS	0.02 +-0.005	0.02 *+-0.004	0.01 +-0.005	0.02 +-0.004	0.01 +-0.004

* Significantly different from control at the 0.05 level of probability.

APPENDIX I

RATS 2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
MALE ORGAN TO BRAIN WEIGHT RATIOS (GMS)
% OF BRAIN WEIGHT

DOSAGE PREDICTED ACTUAL	250 MG/KG (317)	62.5 MG (74.3)	15.6 MG/KG (21.3)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER	909.00 +-89.90	882.70 +-128.70	864.60 +-102.50	755.00 *+-84.00	995.90 +-127.00
KIDNEY	168.46 +-13.70	162.93 +-12.40	153.78 +-21.90	152.38 +-10.20	169.39 +-12.07
SPLEEN	36.71 *+-6.30	51.87 +-13.30	41.86 +-12.00	42.94 +-10.50	51.72 +-6.80
HEART	65.84 *+-7.40	72.23 +-6.40	66.8 +-6.00	65.95 *+-3.70	73.66 +-3.50
TESTES	149.98 +-5.60	149.70 +-11.30	154.13 +-5.90	159.24 +-13.00	158.61 +-12.30
ADRENAL	2.71 +-0.71	2.79 +-0.30	2.43 +-0.57	2.87 +-0.53	2.59 +-0.43

* Significantly different from control at the 0.05 level of probability.

APPENDIX J

RATS 2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
FEMALE
TERMINAL WEIGHTS (GMS)

DOSAGE	PREDICTED ACTUAL	250 MG/KG (206)	125 MG/KG (98.8)	62.5 MG (47.5)	15.6 MG/KG (15.3)	ETHYLACONT (250 MG/KG)	CAGE CONT (0)
LIVER		12.04	11.50	10.85	10.10	10.42	9.80
		**+-0.88	+-1.20	+-1.45	+-1.78	+-1.39	+-1.61
KIDNEY		2.11	2.22	2.02	1.87	2.16	1.91
		+-0.16	+-0.14	+-0.30	+-0.28	+-0.42	0.37
SPLEEN		0.52	0.53	0.58	0.57	0.59	0.54
		+-0.06	+-0.07	+-0.18	+-0.12	+-0.08	+-0.08
HEART		0.90	0.96	0.93	0.90	0.89	0.96
		**+-0.11	+-0.16	+-0.08	+-0.11	+-0.1[illegible]	+-0.08
OVARIES		0.12	0.10	0.12	0.12	0. 2	0.12
		+-0.02	+-0.01	+-0.02	+-0.01	+-0 2	+-0.02
ADRENAL		0.08	0.07	0.08	0.07	0 07	0.07
		+-0.01	+-0.00	+-0.01	+-0.02	+-0 02	+-0.01
BRAIN		1.83	1.83	1.84	1.78	[illegible].83	1.79
		+-0.08	+-0.13	+-0.07	+-0.10	+-[illegible].11	+-0.12
BODY WTS		218.67	233.50	216.67	217.00	21 .17	221.83
		+-17.32	+-21.46	+-41.86	+-26.53	+-2[illegible].70	+-22.07

* Significantly different from control at the 0.05 level of probability.

APPENDIX K

RATS 2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
FEMALE ORGAN TO BRAIN WEIGHT RATIOS (GMS)
% OF BRAIN WEIGHT

DOSAGE	PREDICTED ACTUAL	250 MG/KG (206)	125 MG/KG (98.8)	62.5 MG (47.5)	15.6 MG/KG (15.3)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER		662.56	628.15	589.32	566.84	567.98	547.14
		**+-55.31	**+-32.37	+-80.94	+-96.87	+-57.48	+-69.00
KIDNEY		115.12	122.24	109.38	104.83	117.01	106.71
		+-8.31	+-14.05	+-14.83	+-12.09	+-17.78	15.31
SPLEEN		28.53	29.39	31.76	32.12	31.91	30.40
		+-3.48	+-5.11	+-10.28	+-6.44	+-3.95	+-3.68
HEART		49.45	52.01	50.40	50.21	48.51	54.07
		+-6.92	+-5.75	+-4.57	+-4.40	+-4.95	+-5.26
OVARIES		6.73	5.72	6.69	6.55	6.34	6.62
		+-0.96	+-0.86	+-0.96	+-0.73	+-0.92	+-0.78
ADRENAL		4.37	3.74	4.15	4.22	3.90	3.91
		+-0.82	+-0.45	+-0.55	+-1.26	+-0.83	+-0.61

* Significantly different from control at the 0.05 level of probability.

APPENDIX L

RATS 2-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
FEMALE ORGAN TO BODY WEIGHT RATIOS (GMS)
% OF BODY WEIGHT

DOSAGE PREDICTED ACTUAL	250 MG/KG (206)	125 MG/KG (98.8)	62.5 MG (47.5)	15.6 MG/KG (15.3)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER	5.51	5.21	5.11	4.63	4.59	4.39
	*+-0.20	*+-0.28	+-0.80	+-0.32	+-0.17	+-0.32
KIDNEY	0.96	1.02	0.96	0.86	0.94	0.85
	*+-0.04	*+-0.14	+-0.23	+-0.09	+-0.10	0.09
SPLEEN	0.24	0.25	0.26	0.26	0.26	0.24
	+-0.03	+-0.05	+-0.05	+-0.03	+-0.02	+-0.01
HEART	0.41	0.43	0.44	0.41	0.39	0.43
	+-0.04	+-0.04	+-0.09	+-0.03	+-0.04	+-0.03
OVARIES	0.06	0.05	0.06	0.05	0.05	0.05
	+-0.01	+-0.01	+-0.02	+-0.00	+-0.01	+-0.004
BRAIN	0.84	0.83	0.88	0.83	0.81	0.81
	*+-0.05	+-0.05	+-0.24	+-0.08	+-0.07	+-0.07
ADRENALS	0.04	0.03	0.04	0.03	0.03	0.03
	+-0.01	+-0.00	+-0.01	+-0.01	+-0.01	+-0.00

* Significantly different from control at the 0.05 level of probability.

APPENDIX M

RATS 6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
MALE ORGAN TO BRAIN WEIGHT RATIOS (GMS)
% OF BRAIN WEIGHT

DOSAGE	PREDICTED ACTUAL	250 MG/KG (277.5)	125 MG/KG (128.5)	62.5 MG (69.9)	31.3 MG/KG (37.1)	15.6 MG/KG (20.8)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER		1137.47 +-124.04	1134.89 +-197.07	1021.50 +-194.73	1068.59 *+-98.68	1116.99 +-179.13	1132.63 +-64.60	1199.38 +-60.26
KIDNEY		195.30 +-9.96	204.14 +-17.82	174.65 *+-19.65	184.30 +-19.54	189.85 +-22.22	195.07 +-15.62	+-19.57 +-12.07
SPLEEN		41.26 +-4.46	41.68 +-10.77	44.41 +-15.69	42.62 +-8.97	63.33 +-32.07	55.99 *+-5.05	46.11 +-7.54
HEART		68.36 *+-6.40	71.67 +-5.90	67.89 *+-9.84	75.20 +-4.64	77.80 +-8.23	90.36 *+-7.70	78.39 +-5.55
TESTES		82.45 *+-6.82	104.53 *+-19.51	106.76 *+-6.94	113.48 *+-14.19	122.94 *+-33.17	173.79 +-13.01	176.23 +-9.99
ADRENAL		3.61 +-0.45	3.70 +-0.87	3.73 +-0.28	3.51 +-0.72	3.11 +-0.34	3.92 +-0.55	3.41 +-0.42

* Significantly different from control at the 0.05 level of probability.

APPENDIX N

RATS 6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
MALE
TERMINAL WEIGHTS (GMS)

DOSAGE PREDICTED ACTUAL	250 MG/KG (277.5)	125 MG/KG (128.5)	62.5 MG (69.9)	31.3 MG/KG (37.1)	15.6 MG/KG (20.8)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER	22.56 +-1.94	22.68 +-4.77	21.33 +-3.61	21.79 *+-2.21	23.36 +-4.18	23.08 +-2.30	24.69 +-1.84
KIDNEY	3.88 +-0.19	4.06 +-0.46	3.68 +-0.35	3.76 +-0.43	3.97 +-0.51	3.98 +-0.52	4.10 +-0.34
SPLEEN	0.82 +-0.06	0.84 +-0.25	0.93 +-0.33	0.86 +-0.18	1.33 +-0.72	1.14 *+-0.10	0.95 +-0.15
HEART	1.36 *+-0.09	1.43 *+-0.16	1.42 *+-0.18	1.53 +-0.11	1.62 +-0.16	1.83 *+-0.07	1.61 +-0.07
TESTES	1.64 *+-0.16	2.06 *+-0.28	2.24 *+-0.13	2.31 *+-0.26	2.56 *+-0.69	3.53 +-0.26	3.62 +-0.15
ADRENAL	0.07 +-0.01	0.07 +-0.02	0.08 +-0.01	0.07 +-0.02	0.06 +-0.01	0.08 +-0.01	0.07 +-0.01
BRAIN	1.99 +-0.07	1.99 +-0.14	2.1 +-0.08	2.04 +-0.04	2.09 +-0.07	2.04 +-0.13	2.06 +-0.01
BODY WTS	440.60 *+-14.45	439.50 *+-68.46	436.17 *+-63.85	467.83 +-52.01	482.33 +-51.34	485.40 +-41.92	512.17 +-36.66

* Significantly different from control at the 0.05 level of probability.

APPENDIX O

RATS 6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
MALE ORGAN TO BODY WEIGHT RATIOS (GMS)
% OF BODY WEIGHT

DOSAGE PREDICTED / ACTUAL	250 MG/KG (277.5)	125 MG/KG (128.5)	62.5 MG (69.9)	31.3 MG/KG (37.1)	15.6 MG/KG (20.8)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER	5.12 +-0.46	5.14 +-0.42	4.89 +-0.35	4.67 +-0.40	4.83 +-0.54	4.78 +-0.63	4.83 +-0.39
KIDNEY	0.88 +-0.05	0.93 *+-0.12	0.85 +-0.07	0.80 +-0.06	0.82 +-0.04	0.82 +-0.06	0.8 +-0.08
SPLEEN	0.19 +-0.01	0.19 +-0.03	0.21 +-0.07	0.19 +-0.04	0.27 +-0.13	0.23 *+-0.03	0.18 +-0.02
HEART	0.31 +-0.01	0.33 +-0.03	0.33 +-0.02	0.33 +-0.04	0.34 +-0.02	0.38 *+-0.04	0.32 +-0.03
TESTES	0.38 *+-0.04	0.49 *+-0.15	0.52 *+-0.11	0.50 *+-0.08	0.54 *+-0.15	0.73 +-0.05	0.71 +-0.04
BRAIN	0.45 *+-0.03	0.46 *+-0.05	0.49 *+-0.09	0.44 +-0.04	0.44 0+-0.04	0.42 +-0.03	0.40 +-0.02
ADRENALS	0.02 +-0.00	0.02 +-0.00	0.02 +-0.00	0.01 +-0.00	0.01 +-0.00	0.02 *+-0.00	0.01 +-0.00

* Significantly different from control at the 0.05 level of probability.

APPENDIX P

RATS 6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
FEMALE ORGAN TO BRAIN WEIGHT RATIOS (GMS)
% OF BRAIN WEIGHT

DOSAGE	PREDICTED ACTUAL	250 MG/KG (212.7)	125 MG/KG (108.00)	62.5 MG (56.00)	31.3 MG/KG (31.4)	15.6 MG/KG (16.9)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER		705.4	641.27	564.41	621.59	593.46	578.92	599.35
		+-108.07	+-57.70	+-59.70	+-75.57	+-47.07	+-65.87	+-131.38
KIDNEY		117.45	103.8	104.77	112.99	111.41	112.08	115.59
		+-14.86	+-24.29	+-12.38	+-15.75	+-9.74	+-13.29	+-40.33
SPLEEN		27.25	29.37	28.15	32.53	32.62	33.76	32.79
		+-5.02	+-2.71	+-4.85	+-5.47	+-3.97	+-5.47	+-10.08
HEART		49.91	51.32	47.22	51.98	56.17	55.07	55.79
		+-2.23	+-4.86	+-7.96	+-5.44	+-3.91	+-3.25	+-7.11
OVARIES		6.07	6.7	6.44	7.44	7.71	8.83	8.01
		+-1.05	+-2.29	+-1.24	+-1.40	+-1.39	+-1.93	+-2.92
ADRENAL		4.68	3.92	3.65	4.39	5.53	5.26	4.48
		+-0.60	+-0.67	+-0.86	+-0.63	+-0.54	+-0.93	+-1.85

APPENDIX Q

RATS 6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
FEMALE
TERMINAL WEIGHTS (GMS)

DOSAGE PREDICTED ACTUAL	250 MG/KG (212.7)	125 MG/KG (108.00)	62.5 MG (56.00)	31.3 MG/KG (31.4)	15.6 MG/KG (16.9)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER	13.07 +-2.31	12.22 +-1.53	10.61 +-1.34	11.26 +-1.41	11.01 +-1.48	11.16 +-1.40	11.05 +-2.63
KIDNEY	2.17 +-0.30	1.97 +-0.47	1.97 +-0.30	2.05 +-0.20	2.07 +-0.28	2.16 +-0.24	2.36 +-0.61
SPLEEN	0.50 +-0.09	0.56 +-0.03	0.53 +-0.09	0.59 +-0.09	0.61 +-0.11	0.65 +-0.13	0.6 +-0.20
HEART	0.92 +-0.08	0.97 +-0.10	0.88 +-0.13	0.94 +-0.10	1.04 +-0.09	1.06 +-0.11	1.02 +-0.12
OVARIES	0.11 +-0.02	0.13 +-0.05	0.12 +-0.02	0.13 +-0.03	0.14 +-0.02	0.17 +-0.04	0.15 +-0.06
ADRENAL	0.09 +-0.01	0.07 +-0.02	0.07 +-0.01	0.08 +-0.01	0.10 +-0.01	0.10 +-0.02	0.09 +-0.03
BRAIN	1.85 +-0.10	1.90 +-0.11	1.88 +-0.14	1.81 +-0.07	1.85 +-0.15	1.93 +-0.13	1.84 +-0.10
BODY WTS	250.17 +-27.51	264.00 +-31.05	246.40 +-28.85	261.33 +-20.25	257.20 +-28.42	276.33 +-29.39	286.00 +-33.93

APPENDIX R

RATS 6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
FEMALE ORGAN TO BODY WEIGHT RATIOS (GMS)
% OF BODY WEIGHT

DOSAGE PREDICTED ACTUAL	250 MG/KG (212.7)	125 MG/KG (108.0)	62.5 MG (56.00)	31.3 MG/KG (31.4)	15.6 MG/KG (16.9)	ETHYLACONT (250 MG/KG)	CAGE CONT. (0)
LIVER	5.20 *+-0.44	4.63 *+-0.20	4.30 +-0.09	4.30 +-0.28	4.28 +-0.25	4.04 +-0.27	3.83
KIDNEY	0.86 +-0.04	0.75 +-0.18	0.80 +-0.05	0.78 +-0.06	0.81 +-0.08	0.78 +-0.06	0.73 +-0.20
SPLEEN	0.20 +-0.03	0.21 +-0.03	0.22 +-0.04	0 22 +-0.03	0.24 +-0.02	0.23 +-0.03	0.21 +-0.04
HEART	0.37 +-0.03	0.37 +-0.02	0.36 +-0.02	0.36 +-0.03	0.41 *+-0.03	0.38 +-0.04	0.36 +-0.03
OVARIES	0.04 +-0.01	0.05 +-0.02	0.05 +-0.01	0.05 +-0.01	0.05 +-0.01	0.06 +-0.01	0.05 +-0.02
BRAIN	0.74 *+-0.07	0.72 +-0.07	0.77 *+-0.08	0.70 +-0.05	0.72 *+-0.04	0.70 +-0.07	0.65 +-0.06
ADRENALS	0.03 +-0.01	0.03 +-0.00	0.03 +-0.01	0.03 +-0.00	0.04 +-0.00	0.04 -0.01	0.03 +-0.01

* Significantly different from control at the 0.05 level of probability.

APPENDIX S

6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
CLINICAL CHEMISTRY - MALE RATS

DOSAGE Predicted (Actual)	ALK.PHOS IU/L	SGOT IU/L	SGPT IU/L	GLUCOSE IU/L	T.BILI MG/DL	BUN MG/DL	TOT.PROT. G/DL	CHOLESTEROL IU/L	TRIGLYCERIDES IU/L
250 MG/KG (317)	345.60 +-195.0	70.10 *+-17.8	34.50 +-6.2	149.20 *+-8.4	0.32 *+-0.04	18.00 *+-1.6	6.80 *+-0.3	64.70 *+-17.4	189.50 *+-74.7
125 MG/KG (128.5)	380.30 +-79.4	59.20 *+-6.3	30.80 +-4.1	134.20 *+-7.4	0.36 *+-0.02	17.00 *+-1.2	7.20 +-0.4	61.10 *+-16.1	236.90 *+-12.4
62.5 MG/KG (69.9)	348.80 +-118.4	74.00 *+-9.7	32.00 +-10.3	145.50 *+-22.8	0.48 *+-0.10	20.30 +-2.0	7.50 +-1.0	76.10 *+-12.8	266.40 +-26.7
31.2 MG/KG (37.1)	374.10 +-137.0	111.80 +-24.1	44.40 +-3.8	129.40 +-9.3	0.60 +-0.10	24.90 +-3.8	7.40 +-0.7	76.10 *+-12.1	320.30 +-38.7
15.6 MG/KG (20.8)	440.00 +-125.0	128.50 +-26.7	38.90 +-4.8	125.20 +-16.6	0.56 +-0.10	22.30 +-1.4	7.00 +-0.1	81.70 +-27.6	339.60 +-34.2
ETHYLACET (250 MG/KG)	484.20 +-24.5	121.90 +-30.1	38.00 +-5.8	120.90 +-8.0	0.66 +-0.20	23.50 +-3.3	7.30 +-0.5	83.80 *+-11.5	385.80 +-62.1
CONTROL (0)	381.70 +-118.2	94.70 +-9.2	33.90 +-4.0	113.60 +-14.6	0.61 +-0.10	21.80 +-2.6	7.30 +-0.3	103.00 +-5.3	311.10 +-57.1

* = Statistical significance at the p >0.05 level.
ALK.PHOS.=ALKALINE PHOSPHATASE
SGOT=SERUM GLUTAMIC OXALOACETIC TRANSAMINASE
SGPT=SERUM GLUTAMIC PYRUVIC TRANSAMINASE
GLUCOSE
T.BILL.=TOTAL BILIRUBIN
BUN=BLOOD UREA NITROGEN
TOT.PROT.=TOTAL PROTEIN
CHOLESTEROL
TRIGLYCERIDES

APPENDIX T

6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
CLINICAL CHEMISTRY - FEMALE RATS

DOSAGE Predicted (Actual)	ALK.PHOS IU/L	SGOT IU/L	SGPT IU/L	GLUCOSE IU/L	T.BILI MG/DL	BUN MG/DL	TOT.PROT. G/DL	CHOLESTEROL IU/L	TRIGLYCERIDES IU/L
250 MG/KG	324.60	122.80	40.40	120.10	0.32	18.00	6.80	64.70	189.50
(212.7)	*+-97.00	+-82.80	+-18.40	*+-33.40	*+-0.04	*+-1.6	*+-0.3	*+-17.4	*+-74.7
125 MG/KG	308.30	156.00	34.50	118.60	0.36	17.00	7.20	61.10	236.90
(108.00)	*+-56.80	+-117.30	+-8.80	*+-22.00	*+-0.02	*+-1.2	+-0.4	*+-16.1	*+-12.4
62.5 MG/KG	269.50	136.00	35.90	115.00	0.48	20.80	7.50	76.10	266.40
(56.00)	+-69.50	+-89.80	+-11.10	*+-19.80	*+-0.10	+-2.0	+-1.0	*+-12.8	+-26.7
31.2 MG/KG	237.10	139.30	36.50	131.60	0.60	24.90	7.40	76.10	320.30
(31.4)	+-87.80	+-157.10	+-11.20	*+-4.30	+-0.10	+-3.8	+-0.7	*+-12.1	+-38.7
15.6 MG/KG	189.60	102.90	48.12	141.80	0.56	22.30	7.00	81.70	339.60
(16.9)	+-97.60	+-36.80	+-19.40	*+-10.80	+-0.10	+-1.4	+-0.1	+-27.6	+-34.2
ETHYLACET	208.80	70.40	29.10	147.50	0.66	23.50	7.30	83.80	385.80
(250 MG/KG)	+-75.40	+-14.60	*+-3.40	*+-6.90	+-0.20	+-3.3	+-0.5	*+-11.5	+-62.1
CONTROL	197.90	68.00	36.40	169.70	0.61	21.80	7.30	103.00	311.10
(0)	+-66.20	+-18.93	+-7.10	+-18.50	+-0.10	+-2.6	+-0.3	+-5.3	+-57.1

* = Stratistical significance at the p >0.05 level.
ALK.PHOS.=ALKALINE PHOSPHATASE
SGOT=SERUM GLUTAMIC OXALOACETIC TRANSAMINASE
SGPT=SERUM GLUTAMIC PYRUVIC TRANSAMINASE
GLUCOSE
T.BILL.=TOTAL BILIRUBIN
BUN=BLOOD UREA NITROGEN
TOT.PROT.=TOTAL PROTEIN
CHOLESTEROL
TRIGLYCERIDES

APPENDIX U

6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
HEMATOLOGY - FEMALE RATS

DOSAGE Predicted (Actual)	RBC 10/µl	HCT %	MCV fl	WBC 10/µl	HGB g/dl	MCH pg	MCHC g/dl
250 MG/KG (217.7)	6.32 *+-0.19	36.47 *+-1.07	57.77 *+-1.33	8.63 +-3.53	13.08 *+-0.44	20.72 *+-0.54	35.85 *+-0.32
125 MG/KG (108.00)	6.92 +-0.42	38.43 +-2.29	55.60 +-1.29	11.35 *+-3.01	13.82 +-0.89	19.98 +-0.37	35.93 *+-0.55
62.5 MG/KG (56.00)	7.14 +-0.49	39.14 +-1.81	54.90 +-1.75	10.30 *+-2.67	14.10 +-0.64	19.78 +-0.86	36.06 *+-0.49
31.3 (31.4)	7.80 +-0.29	42.27 +-1.68	54.20 +-0.72	13.20 *+-4.54	15.22 +-0.57	19.53 +-0.37	35.83 +-0.80
15.6 MG/KG (16.9)	7.50 +-0.28	41.84 +-2.18	55.76 +-1.15	11.74 *+-5.07	15.10 +-0.84	20.14 +-0.43	36.08 *+-0.53
ETHACET.CON (250)	7.53 +-0.39	40.93 +-1.93	54.42 +-1.98	13.05 *+-2.17	14.77 +-0.32	19.62 +-0.87	36.07 *+-0.42
CONTROL (0)	7.47 +-0.53	41.40 +-2.64	55.48 +-1.33	6.78 +-1.52	14.52 +-0.73	19.48 +-0.60	35.08 +-0.61

RBC = RED BLOOD CELLS
HGB = HEMOGLOBIN
HCT = HEMATOCRIT
MCV = MEAN CELL VOLUME
MCH = MEAN CELL HEMOGLOBIN

APPENDIX V

6-WEEK GAVAGE FEEDING STUDY
DANPE
STUDY NO. 75-51-Y809-90
HEMATOLOGY - MALE RATS

DOSAGE Predicted (Actual)	RBC 10/µl	HCT %	MCV fl	WBC 10/µl	HGB g/dl	MCH pg	MCHC g/dl
250 MG/KG (277.5)	6.96 *+-0.38	37.28 *+-1.47	53.66 +-2.51	17.86 *+-2.62	13.52 *+-0.23	19.46 +-0.89	36.26 +-0.21
125 MG/KG (128.5)	7.62 +-0.40	40.46 +-3.54	53.18 +-2.46	16.52 *+-4.62	14.44 +-1.17	18.96 +-0.81	35.70 +-0.29
62.5 MG/KG (69.9)	7.68 +-0.33	40.18 +-1.74	52.74 +-0.75	19.56 *+-4.79	14.42 +-0.60	18.96 +-0.34	35.90 +-0.19
31.3 (37.1)	7.85 +-0.43	40.98 +-1.40	52.27 +-1.84	17.47 *+-6.75	14.65 +-0.45	18.68 +-0.62	35.77 +-0.51
15.6 MG/KG (20.8)	7.43 +-0.41	39.73 +-2.16	53.47 +-0.67	16.32 *+-4.31	14.45 +-0.72	19.45 +-0.38	36.37 +-0.45
ETHACET.CON (250)	7.85 +-0.31	41.97 +-1.20	53.47 +-0.67	20.63 *+-6.73	14.92 +-0.54	19.03 +-0.09	35.58 +-0.33
CONTROL (0)	7.48 +-0.13	39.97 +-0.97	53.42 +-1.53	13.52 +-1.71	14.28 +-0.39	19.10 +-0.47	35.75 +-0.99

RBC = RED BLOOD CELLS
HGB = HEMOGLOBIN
HCT = HEMATOCRIT
MCV = MEAN CELL VOLUME
MCH = MEAN CELL HEMOGLOBIN